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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/628,879	SEKAR ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment of claim 1 is acknowledged and has been entered.

Rejections Withdrawn

2. Applicant's arguments, see pgs. 4-5, filed November 11, 2004, with respect to the rejections under 35 U.S.C. 112, second paragraph, have been fully considered and are persuasive. The rejections of claims 1-21 under 35 U.S.C. 112, second paragraph, has been withdrawn.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1, 8, 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Potyrailo et al [Potyrailo et al, Adapting selected nucleic acid ligands to biosensors, 1998, Anal Chem 70:3419-3425].

With respect to claim 1, Potyrailo et al teach an anti-thrombin DNA aptamer (p.3419, col.1) immobilized to a glass surface (p.3420, col.1) and the use of fluorescence anisotropy to

detect the bound labeled aptamer probe-analyte binding event using a vertically polarized laser (p.3420, col.2). Potyrailo et al further teaches that the illumination can be performed with direct sample illumination, although Potyrailo et al further specifies that evanescent wave is more advantageous than direct sample illumination (p.3422, col.2, lines 37-43).

5. With respect to claim 8, the aptamers comprise 15-mer single-stranded DNA that bind to the blood-clotting factor thrombin (p.3421, col.2).

6. With respect to claim 16, a vertically polarized laser is used to detect fluorescence anisotropy (p.3420, col.2).

7. Claims 1, 17-19, 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Fang et al [Fang et al, Molecular aptamer for real-time oncoprotein platelet derived growth factor monitoring by fluorescence anisotropy, 2001, Anal Chem, 73, 5752-5757].

With respect to claim 1, Fang et al teach the detection of oncoprotein PDGF, a potential protein marker for cancer diagnosis (p.5753, col.1) using fluorescence anisotropy, where fluorescence measurements were performed on a spectrofluorometer after illumination with polarized light (p.5753, col.2). Fang et al further teach that the detection of PDGF using fluorescence anisotropy is expected to be sensitive, convenient, and selective (p.5753, col.2), and is quick and can detect PDGF down to 0.22 nM (p.5757, col.1). Fang et al further teach that this assay component can be used for biosensors by immobilization of the aptamer onto a solid surface (p. 5757, col.2, lines 3-7).

8. With respect to claim 17-19, 21, Fang et al teach the detection of oncoprotein PDGF, a potential protein marker, for developing an assay for cancer diagnosis (p.5753, col.1).

9. Claims 1, 2, 7-9, 11-21 rejected under 35 U.S.C. 102(e) as being anticipated by Stanton et al [US 6,680,377].

With respect to claim 1, Stanton et al teach aptamer beacons comprising aptamers configured to bind to specific target molecules (column 8, lines 14-15) which can be attached to a solid support at different predetermined points in a one or two-dimensional array (column 2, lines 7-15) such as a particle or a plate (column 4, lines 5-10). Upon binding of the aptamer beacon to a target molecule, concomitant signals such as fluorescence anisotropy can be generated (column 9, lines 59-65).

10. With respect to claims 2, 7, 11, the aptamers can be attached to a solid support at different predetermined points in a one or two-dimensional array (column 2, lines 7-15) such as a particle or a plate (column 4, lines 5-10).

11. With respect to claim 8, the aptamers can comprise between 10-100 nucleotides (column 24, lines 14-24).

12. With respect to claim 9, the aptamers can be labeld to fluorescein or rhodamine (column 13, lines 49-51).

13. With respect to claim 12-13, the aptamers can be configured to bind to specific target molecules (column 8, lines 14-15) which can be attached to a solid support at different predetermined points in a one or two-dimensional array (column 2, lines 7-15) such as a particle or a plate (column 4, lines 5-10). Different spots would contain a plurality of identical aptamer beacons (column 4, lines 9-12).

14. With respect to claims 14, 15, a plurality of different aptamer beacon species could be bound to the support with different fluorescent dyes to allow for simultaneous detection of multiple target molecules (column 5, lines 31-53).

15. With respect to claim 16, a high intensity source such as a laser may be used (column 5, lines 54-61).

16. With respect to claims 17-18, 21, the detection systems can be used for testing for the presence or absence of a disease and monitoring the progression of a disease such as cancer (column 18, lines 5-15).

17. With respect to claim 19, the aptamers may bind to different surface proteins of bacteria (column 5, lines 1-5).

18. With respect to claim 20, the aptamers may be configured to detect the metabolites of another drug (column 11, lines 54-65).

19. Claims 1, 9-10, 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Lakowicz et al [US 5,631,169].

With respect to claim 1, Lakowicz et al teach a fluorometric luminescence immunoassay comprising the steps of exciting a sample with radiation from any suitable radiation source such as a laser (polarized light) (column 2, lines 55-60), where the sample comprises a reactant bound to polymeric supports and a second reactant supplied to the support in solution or suspension (column 2, lines 45-55). Anisotropy or polarization are properties which can be used to detect the lifetime change, as well as the amount of the reaction product, and thus the concentration of either of the reactants (column 2, lines 30-38).

20. With respect to claims 9-10, Lakowicz et al teach aptamers with carboxyfluorescein donors (column 4, lines 8-11).

21. With respect to claim 16, the radiation source is a laser (column 2, lines 55-60).

22. Claims 1, 9, 11, 12, 14, 17-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Gold et al [US 6,544,776] in light of Fang et al [Fang et al, Molecular aptamer for real-time oncoprotein platelet derived growth factor monitoring by fluorescence anisotropy, 2001, 73, 5752-5757].

With respect to claim 1, Gold et al teach aptamers immobilized to the surface of biochips (column 10, lines 60-67), and measurement of fluorescence anisotropy to determine presence of target molecules (column 16, lines 15-36).

Although Gold et al, do not teach illuminating the aptamer with polarized light to measure the amount of fluorescence anisotropy, a person of ordinary skill in the art would know that the use of polarized light is required, as shown by Fang et al, who teaches that the measurement of fluorescent anisotropy is based on the simple principle of fluorescence illumination using polarized light (p.5754, col.2, lines 11-19). Fang et al further teach that this assay concept can also be applied biosensors by immobilization of the aptamer onto a solid surface (p.5757, col.2, lines 3-6), such as in Gold et al.

23. With respect to claim 9, Gold et al teach the use of fluorescein (column 12, lines 16-20).

24. With respect to claims 11-12, Gold et al teach a 4x4 array of aptamers (fig. 1, column 3, lines 28-38).

25. With respect to claim 14, Gold et al teach an array of photoreactive aptamers, where irradiation will covalently attach only the correct protein to the correct photoactivitable aptamer present at a defined area of a matrix laid out on the surface of the chip (column 18, lines 14-20).

26. With respect to claims 17, 18, 21, Gold et al teach that the attached nucleic acid ligands will bind to components of the blood plasma or other bodily fluid of an individual known to be suffering from a particular disease where the target molecules are not found in the bodily fluid of healthy individuals (col. 2, line 65 – col. 3, line 11).

27. With respect to claims 19-20, Gold et al teach that the target molecule can be a protein or metabolite (column 4, lines 45-58).

Claim Rejections - 35 USC § 103

28. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

29. Claims 2-9, 11-13, 17-19, 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fang et al [Fang et al, Molecular aptamer for real-time oncoprotein platelet derived growth factor monitoring by fluorescence anisotropy, 2001, 73, 5752-5757] in view of Lee et al [Lee et al, A fiber-optic microarray biosensor using aptamers as receptors, 2000, Anal Biochem, 282:142-146].

With respect to claims 2-3, Fang et al teach the detection of oncoprotein PDGF, a potential protein marker for cancer diagnosis (p.5753, col.1) using fluorescence anisotropy,

where fluorescence measurements were performed on a spectrofluorometer after illumination with polarized light (p.5753, col.2). Fang et al further teach that the detection of PDGF using fluorescence anisotropy is expected to be sensitive, convenient, and selective (p.5753, col.2), and is quick and can detect PDGF down to 0.22 nM (p.5757, col.1). Fang et al further teach that this assay component can be used for biosensors by immobilization of the aptamer onto a solid surface (p. 5757, col.2, lines 3-7). Fang et al, however, do not specify that the aptamers are silica beads.

Lee et al, however, do teach a method of measuring an analyte using a system comprising DNA aptamers immobilized on the surface of silica beads (p. 143, col. 1) and making fluorescent measurements. Lee et al further teaches that this system shows selectivity for its target and can be reused with good reproducibility, allows for the possibility for multianalyte detection (p. 146, col. 1, lines 19-30).

Therefore it would have been obvious in the method of Lee et al to measure fluorescence anisotropy, as suggested by Fang et al, in order to provide an assay for onco-protein and disease related protein detection that is quick, sensitive, convenient, and selective.

30. With respect to claims 2-3, the beads taught by Lee et al are silica (p. 143, col.1).

31. With respect to claims 4-5, the beads taught by Lee et al have a diameter of 3.1μm (p.143, col.1).

Furthermore, although Lee et al do not teach beads with a diameters of 5μm, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranged involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

32. With respect to claim 6, Lee et al teach that F-thrombin was diluted with PBS, and 10μL of each concentration was brought to the fiber's distal end (where the beads are located) and incubated from 8 min (p.143, col.2).

33. With respect to claim 7, 11, the beads with attached aptamers taught by Lee et al are arranged on microwell arrays (p. 143, col.2).

34. With respect to claim 8, Lee et al teach that the aptamers are 15-mer single stranded DNA that bind to thrombin (p.143, col.1).

35. With respect to claim 9, the aptamers used by Lee et al are labeled with fluorescein phosphoramidite (pl 143, col.1).

36. With respect to claim 12, the biosensor array taught by Lee et al contains multiple microwells containing the beads (p. 143, col.2).

37. With respect to claim 13, each addressable location of the biosensor taught by Lee et al comprises thrombin aptamer beads (p. 144, col.2).

Response to Arguments

38. Applicant's arguments with respect to claims 1-21 have been considered but are moot in view of the new ground(s) of rejection. The following arguments made by applicant, however, will be addressed as they apply to the prior art in the new rejections as well.

39. With respect to applicant's argument on pgs 5-6 that Potyrailo et al does not teach direct illumination of the fluorophore, it should be noted that Potyrailo et al does in fact compare direct sample illumination to evanescent wave as discussed above. Although Potyrailo et al teach that it is more advantageous to use evanescent wave, all embodiments of the invention disclosed in the prior art must be considered, and therefore the claims would still read upon the prior art.

40. With respect to applicant's argument on pgs 6-9 regarding Fang et al and Gold et al in that Fang et al teach a method of solution based measurement of anisotropy and do not teach a support based measurement of anisotropy, and therefore would not be compatible with the method taught by Gold et al, it should be noted that Fang et al do teach that their method of solution based measurement of anisotropy would in fact applicable in support based methods, such as biosensors, where immobilization of the aptamer onto a solid surface occurs, as discussed above. This is also applicable to applicant's arguments regarding Fang et al and Lee et al on pgs 10-12.

Conclusion

41. No claims are allowed.

42. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

43. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

44. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

45. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nelson Yang
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1/19/05